EXHIBIT L

VARIAN medical systems

Case Study | Lung Stereotactic Body Radiation Therapy

LUNG STEREOTACTIC BODY RADIATION THERAPY WITH HIGH INTENSITY MODE ON A CLINAC iX

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Introduction

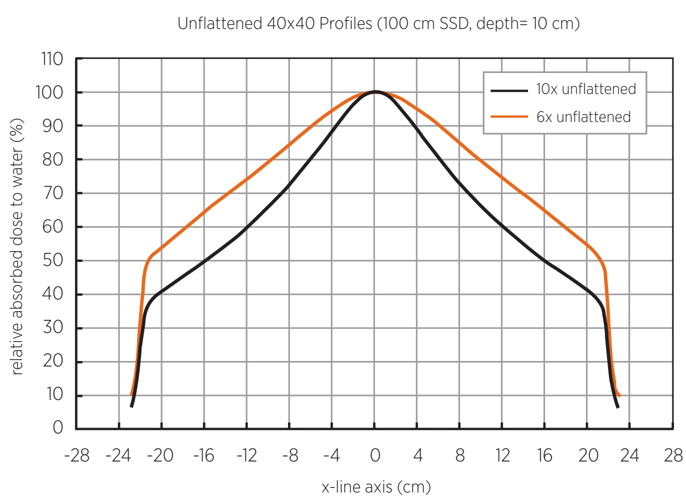
At Panhandle Cancer Care Center, we treat many cases using a combination of the RapidArc® radiotherapy technology technique and the 6 MV X-ray flattening filter free (6X) beam in High Intensity Mode (HIM). By removing the flattening filter, the Varian Clinac® iX linear accelerator generates a beam characterized by a very high dose rate on the central beam axis, with rapidly decreasing intensity moving away from the beam center (see Figure 1). HIM beams are of interest for radiation treatment because they may offer the potential for fast treatment delivery without compromising plan quality or accuracy of dose delivery.[1] In addition, HIM may also reduce out-of-field dose, head scatter, and leakage dose through the multileaf collimator (MLC).[2]

For the 6X beam, HIM can achieve a maximum dose rate of 1400 monitor units per minute (MU/min). Using HIM, we have been able to achieve optimal dose distributions in intensity modulated treatments with a single rotation of the gantry. Our primary objectives for using HIM with RapidArc are to shorten the beam-on time, minimize the time the patient spends on the table, and thereby maximize delivery accuracy by reducing the risk and impact of intrafraction patient movement.[3] Other potential benefits are a more comfortable patient experience and higher efficiency in patient throughput.

Since acquiring the Varian Clinac iX with HIM, we have treated 30 patients with HIM, including prostate, brain, esophagus, and lung cases. The case described here is a lung treatment.

Figure 1

Beam profiles without the flattening filter



Case Report

A highly functioning, cooperative 87-year-old female was diagnosed with an inoperable T2a, N3, M0, non-small-cell lung carcinoma. Following chemotherapy, a PET/CT scan showed a residual mass in the periphery of the left lower lobe that measured 1.6 cm x 1.1 cm x 2.0 cm (see Figure 2).

Figure 2

PET/CT diagnostic image

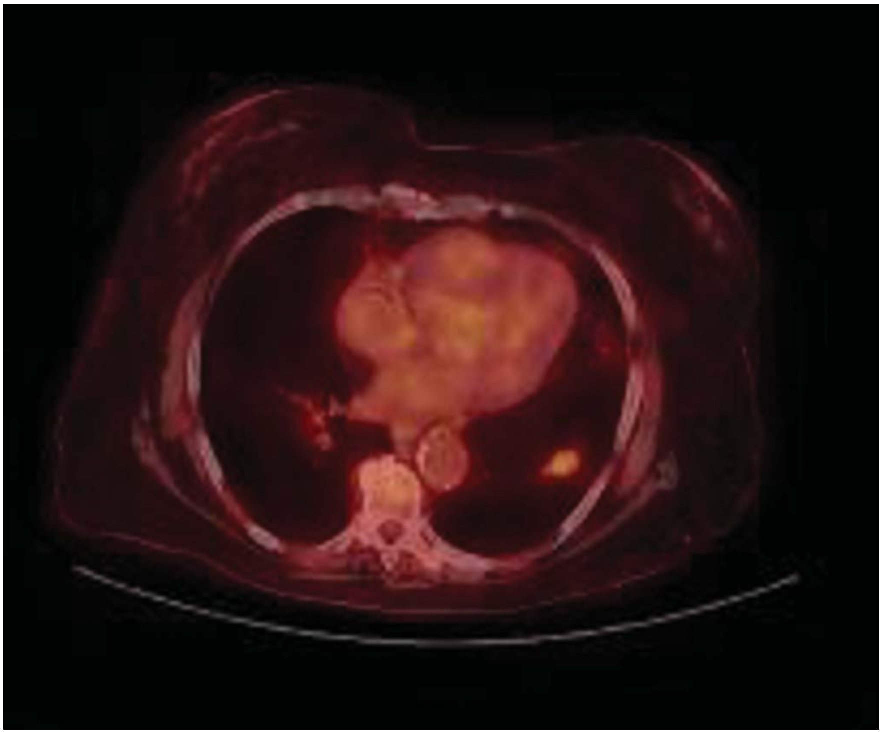
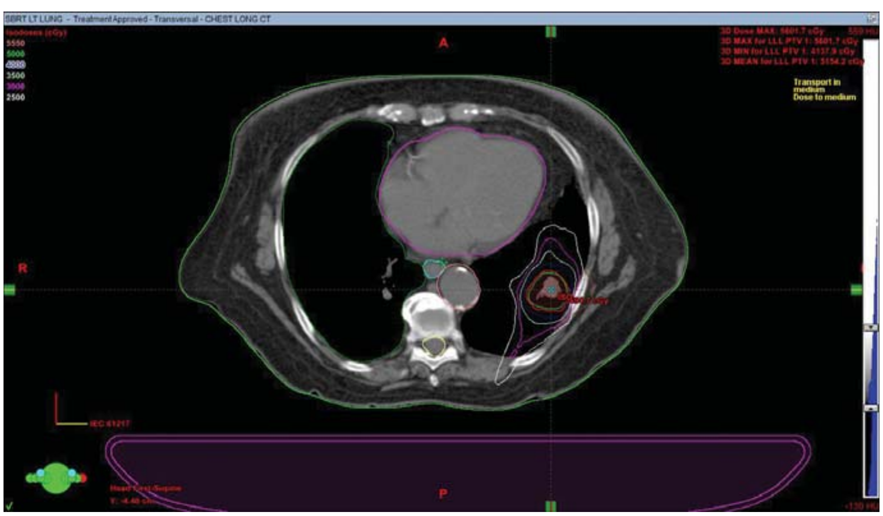


Figure 3

Image-guided dosimetric assessement of HIM RapidArc plan. The treatment was planned to minimize dose and avoid the chest wall sector.



Treatment Simulation

The patient was simulated in the head-first supine position with her hands above her head on a CT Scanner. She was immobilized using a Vac-Lok™ bag. We performed an inspiration breath-hold CT scan and a free-breathing CT scan. These images were fused with the PET/CT utilizing Eclipse™ treatment planning system Version 11.

Treatment Planning

An internal target volume (ITV) was generated utilizing CT and PET/CT imaging techniques and drawn to the furthest extent of the tumor motion. The planning target volume (PTV) was created by expanding the ITV by 0.5 cm in all transverse directions and 1.0 cm superiorly and inferiorly, in accordance with RTOG 0236. The resulting PTV volume was 46.1 cc (see Figure 3).

We generated two plans for comparison, for delivering a prescribed dose of 5000 cGy in five 1000-cGy fractions (see Figure 4). Plan 1 was a two-arc isotropically distributed plan utilizing the 6X beam in standard mode. However, dose to the chest wall exceeded the 4300-cGy maximum recommended by AAPM Task Group 101.[4] Plan 2 was single-arc plan utilizing 6X HIM with an avoidance sector on the chest wall to reduce the risk of rib fracture. Plan 2 provided a maximum dose to the chest wall that is well below the 4300 cGy guideline. Both plans were calculated using the Acuros® XB algorithm (see Figure 5).

Treatment Delivery

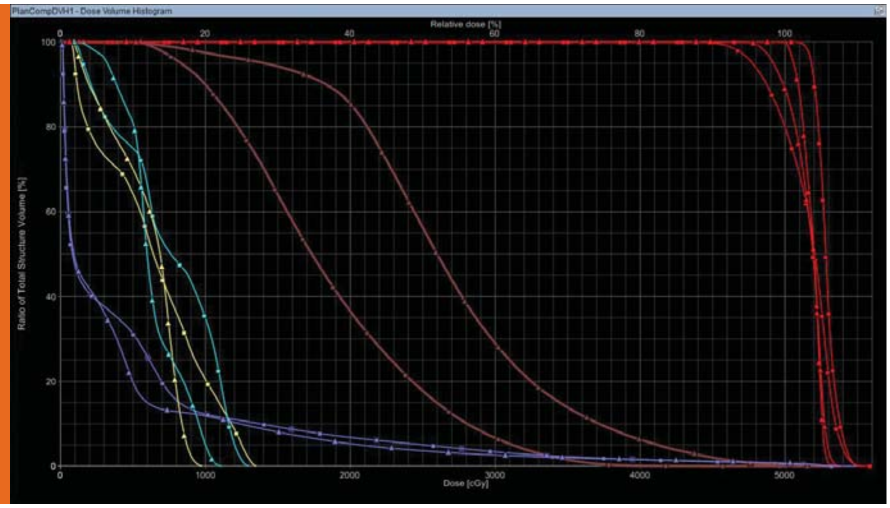
The patient was brought in before the start of treatment for a simulation on the Clinac iX system with advanced imaging to verify positioning and to validate the PTV using cone-beam CT (CBCT) and kV fluoroscopic imaging. A slow CBCT imaging protocol was used to capture the full extent of tumor motion throughout several breathing cycles. The CBCT was registered with the planning CT to assure the captured CBCT tumor motion remains within the created PTV margins used during the planning process

For treatment, the patient was immobilized using a Vac-Lok™ bag. She was allowed to free breath, and no abdominal compression

Figure 4

Dose-volume histogram comparing Plan 1 with HIM and Plan 2 without HIM.

- ▲ **Plan 1, Plan with 6MV HIM beam using a single arc and avoiding the chest wall**
- ■ **Plan 2, Standard 6MV plan used as a baseline. This plan was developed with two isotropic arcs and little to no optimization to avoid adjacent structures. This plan would represent the best case scenario for homogeneous coverage to the PTV and would have been deemed acceptable if not for the dose to the chest wall.**



was applied. The patient was treated using RapidArc with the 6X HIM beam, at a dose rate of 1400 MU/min. For the 6X beam, HIM can achieve a maximum dose rate of 1400 MU/min, though gantry speed and collimator leaf speed ultimately affects realized dose rate. The total beam-on time for each treatment session was 2.5 minutes, compared to about 6 minutes, which would have been required for treatment without the HIM beam.

Observations and Results

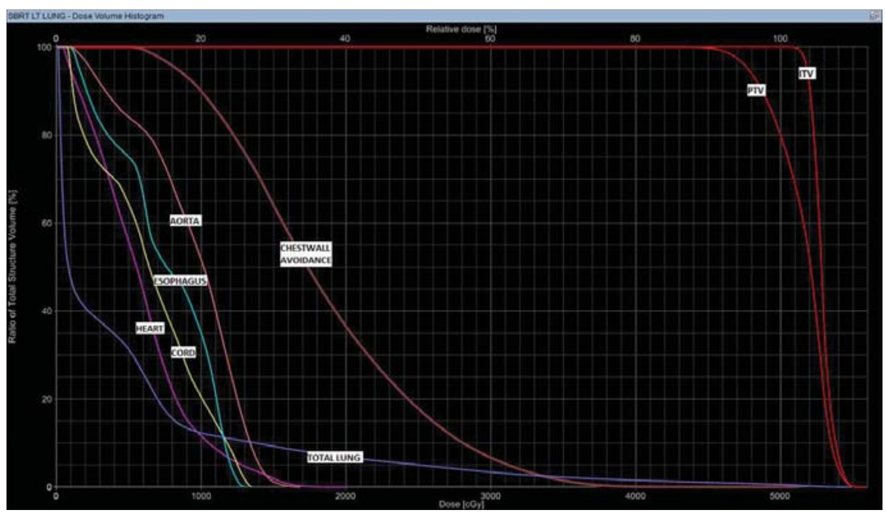
At the one-month follow-up, the patient's breathing was unlabored, and she was easily able to take a deep breath. In addition, she exhibited no skin effects or other short-term side effects of the radiation treatment. At three-month follow up, her CT scan was inconclusive. Though the lesion did not initially appear reduced in size, the CT scan alone cannot reveal if the remaining mass is tumor or the result of scarring.

The Varian HIM beam provided a considerable decrease in the treatment time, which may make treatment more tolerable for some patients and potentially decrease the risk of intrafraction motion.

Our experience with HIM in this and other cases suggests it would be useful for radiosurgery, stereotactic body radiotherapy, and respiratory-gated or breath-hold treatment techniques.

Figure 5

Dose-volume histogram for HIM RapdiArc plan used for SBRT LT Lung showing reduction of dose to the adjacent chest wall to reduce potential rib fracture.



Panhandle Cancer Care Center

Panhandle Cancer Care Center (PC³), located in Amarillo, Texas, provides radiation therapy services for the entire Texas Panhandle as well as parts of New Mexico, Colorado, Kansas and Oklahoma. PC³ treats all cancer sites using VMAT, IGRT, SBRT and conventional 3D plans on a Varian Clinac iX® accelerator.

The accelerator is equipped with 6 and 15 MV photon beams, a 6 MV Flattening Filter Free beam and four electron beams of 6,9,12, and 15 MeV. PC³ is an all Varian, paperless environment utilizing Aria® oncology information system and Eclipse™ treatment planning system Version 11.

References

1) Ong CL, Verbakel WF, et al, Fast arc delivery for stereotactic body radiotherapy of vertebral and lung tumors, Int. J. Radiat. Onco.l Biol. Phys.. 2012 May 1;83(1).
2) Cho W, Kielar KN, et al, Multisource modeling of flattening filter free (FFF) beam and the optimization of model parameters, Med. Phy.s. 2011 Apr;38(4):1931-42.
3) Purdie TG, Bissonnette JP, et al, Cone-beam computed tomography for on-line image guidance of lung stereotactic radiotherapy: Localization, verification, and intrafraction tumor position, Int. J. Radiat. Oncol. Biol. Phys. 2007 May;68(1):243-252
4) Benedict SH, Yenice KM, et al, Stereotactic body radiation therapy: The report of AAPM Task Group 101, Med. Phys. 2010 Aug;37(8):4078-4101.

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Intended Use Summary

Varian Medical Systems' linear accelerators are intended to provide stereotactic radiosurgery and precision radiotherapy for lesions, tumors, and conditions anywhere in the body where radiation treatment is indicated.

Safety

Radiation treatments may cause side effects that can vary depending on the part of the body being treated. The most frequent ones are typically temporary and may include, but are not limited to, irritation to the respiratory, digestive, urinary or reproductive systems, fatigue, nausea, skin irritation, and hair loss. In some patients, they can be severe. Treatment sessions may vary in complexity and time. Radiation treatment is not appropriate for all cancers.

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